INTERVIEW SUMMARY

A telephonic interview was conducted on June 18, 2007. Applicant thanks the Examiner for the courtesy of granting the interview. Participating in the interview were Examiner Frank Wu and Applicant's Attorney John Burns. Examiner Wu and Attorney Burns discussed possible claim amendments and cancellations in light of some of the cited references. No agreement was reached.

REMARKS

Status of the Claims

Claims 15, 23, and 24 are canceled. Applicant reserves the right to pursue the subject matter of these claims in subsequent prosecution. Claims 1, 16, 18, 21, and 25 have been amended. Thus, Claims 1-14, 16-22, and 25-34 are currently pending.

Support for language of amended Claim 1 is found in originally filed Claims 15 and 25 and throughout the specification, for example, at Example 3 "RNA*later* Treatment Preserves RNA in Fractionated WBCs" and Example 4 "RNA*later* Treatment Reduces Genomic DNA Contamination". Claims 16, 18, 21, and 25 have been amended to change their dependency. Therefore, no new matter is added by the amendments.

Rejection Under 35 USC § 102 (a) or (e) and Traverse

Claims 1-4, 7, 8, 10, 11, 14, and 29 were rejected for allegedly being anticipated by Garvin (US2003/0170669). See the Office Action at pages 2-3.

To anticipate a claim, each and every element of the claim must be found in a single prior art reference. MPEP §2131. Independent Claim 1, as amended, recites in part: "treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and (i) increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and (ii) reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition;" and obtaining a lysate comprising RNA "and reduced gDNA contamination ...". Applicant respectfully asserts that Garvin lacks the recited elements of amended independent Claim 1. Garvin lacks any teaching or suggestion of an RNA preservation composition of the current teachings nor obtaining RNA from a white blood cell lysate comprising reduced gDNA contamination. Since Garvin lacks any teaching of independent claim 1, Garvin cannot anticipate Claim 1.

An essential characteristic of a proper dependent claim is that it include every limitation of the claim from which it depends. Therefore, a dependent claim is allowable when the claim

from which it depends is allowable. Claims 2-4, 7, 8, 10, 11, 14, and 29 depend either directly or indirectly from Claim 1. Hence, these rejections are moot and Applicant respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. §103 (a) and Traverse

Claim 9 was rejected as being unpatentable over Garvin as applied to Claims 1-4, 7, 8, 10, 11, 14, and 19 and further in view of Rutter *et al.* (U.S. Patent No. 4,652,525). See Office Action at pages 4-5. Claims 5 and 6 were rejected as being unpatentable over Garvin in view of Rutter *et al.* and further in view of Ala-Kokko *et al.* See Office Action at pages 5-6. Claims 12, 13, and 26 were rejected as unpatentable over Garvin in view of Maniatis *et al.* See Office Aetion at pages 6-7. Claims 15-18, 23, and 28 were rejected as being unpatentable over Garvin in view of Korfhage *et al.* (U.S. Patent No. 6,872,818). See Office Action at pages 7-8. Claims 15-23 and 28 were rejected as being unpatentable over Garvin in view of Lader (US Patent No. 6,204,375). See Office Action at pages 9-11. Claims 24, 25, and 27 were rejected as unpatentable over Garvin in view of Korfhage *et al.* or over Garvin in view of Lader and further in view of Maniatis *et al.* See Office Action at pages 11-12. Claims 30-34 were rejected as being unpatentable over Garvin in view of Warrington *et al.* (U.S. Patent No. 7,108,969). See Office Action at pages 12-13. Applicant respectfully traverses these rejections.

Claims 15, 23, and 24 have been canceled. Amended Claim 1, a method for obtaining a leukocyte lysate comprising RNA and reduced genomic DNA contamination, currently recites among other things, treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes to reduce the gDNA contamination in the subsequent lysate compared to a lysate of fractionated leukocytes that were not treated with the RNA preservation composition.

In *KSR International Co. v. Teleflex Inc.* U.S. No. 04-1350, April 30, 2007, the Supreme Court reiterated that the framework for determining obviousness under §103 it had set out in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) continues to "define the inquiry that controls" determination of obviousness or nonobviousness of the claimed subject matter. As set forth in *Graham*, obviousness under 35 U.S.C. §103 is a question of law based on factual inquiries: (1) the scope and the content of the prior art; (2) the differences between the prior art

and the claims at issue; (3) the level of ordinary skill in the art, and (4) objeetive evidence of secondary considerations. In *KSR*, the Supreme Court cited that secondary considerations might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

Scope and Content of the Prior Art

Garvin, U.S. Published Patent Application No. 2003/0170669, relates to methods for recovering nucleic acids characterized by the steps of (a) filtering blood through a filter medium selectively adsorbing nucleated cells; (b) separating the material retained on filtering by the filter medium at least partly from the filter medium; and (c) isolating nucleic acids from the material separated from the filter medium. Garvin is silent regarding reducing genomic DNA (gDNA) contamination of a leukocyte lysate by treating fractionated leukocytes with an RNA preservation composition.

The Rutter *et al.* (U.S. Patent No. 4,652,525) document is cited by the Action for disclosing isolation of mRNA by homogenizing a cell preparation in guanidinium thiocyanate buffered to low pH and containing mercaptoethanol. The Rutter *et al.* document is silent regarding reducing genomic DNA (gDNA) contamination of a leukoeyte lysate by treating fractionated leukoeytes with an RNA preservation composition.

The Ala-Kokko *et al.* document, U.S. Patent No. 5,045,449, is cited by the Action for disclosing isolation of total RNA using a lysis solution comprising sarcosyl and guanidinium (sic) thiocyanate. The Ala-Kokko *et al.* document is silent regarding reducing genomic DNA (gDNA) contamination of a leukocyte lysate by treating fractionated leukocytes with an RNA preservation composition.

Maniatis *et al.* (Molecular Cloning: A Laboratory Manual, pages 191-193, 1982) teach removal of protein via phenol/chloroform and removal of DNA using shearing and DNase I (page 192). The Maniatis *et al.* document is silent regarding reducing genomic DNA (gDNA) contamination of a leukocyte lysate by treating fractionated leukocytes with an RNA preservation composition.

The Korfhage *et al.* document (U.S. Patent No. 6,872,818) is cited by the Action for disclosing use of ammonium sulfate to mitigate or neutralize inhibitory effects of certain molecules that interfere with RNA function or to reduce the detrimental effects of some agents

on RNA activity. The Korfhage *et al.* document is silent regarding reducing genomic DNA (gDNA) contamination of a leukocyte lysate by treating fractionated leukocytes with an RNA preservation composition.

The Lader document (U.S. Patent No. 6,204,375) is cited by the Action for disclosing an RNA preservation medium comprising ammonium sulfate. Lader is silent regarding reducing genomic DNA (gDNA) contamination of a leukocyte lysate by treating fractionated leukocytes with an RNA preservation composition.

The Warrington *et al.* (U.S. Patent No. 7,108,969) document is cited by the Action for disclosing examination of quality and quantity of isolated RNA by RT-PCR and microarray analysis. The Warrington *et al.* document is silent regarding reducing genomic DNA (gDNA) contamination of a leukocyte lysate by treating fractionated leukocytes with an RNA preservation composition.

Differences Between the Cited Art and the Claims at Issue

Applicant respectfully submits that none of the prior art references cited by the Office Action teach or suggest treating fractionated leukocytes with an RNA preservation composition to reduce gDNA contamination in the subsequent lysate, as recited in Claim 1 upon which the rejected claims depend, either directly or indirectly.

The level of ordinary skill in the art

The level of ordinary skill in the art is considered to be a graduate student or post-doctoral fellow in a biological science. According to KSR at page 17, a person of ordinary skill is also a person of ordinary creativity.

Based upon any combination of Garvin with Rutter *et al.*, Ala-Kokko *et al.*, Maniatis *et al.*, Korfhage *et al.*, Lader, or Warrington *et al.*, as cited above, one of ordinary skill in the art would not have found it obvious to selectively pick and choose elements from the references so as to arrive at the claimed invention without using the claims as a guide. Selectively picking and

choosing elements of prior art based on the claims is improper hindsight analysis that reads into the art Applicants' own teachings.

Other criteria for establishing a *prima facie* case of obviousness relied upon include the so-called teaching-suggestion-motivation test which the Supreme Court found in *KSR* to be not necessarily inconsistent with the *Graham* analysis. For this test, three basic criteria are analyzed: the prior art reference (or references when combined) are analyzed for (1) a teaching or suggestion of all the claim limitations; (2) some suggestion or motivation, either in the referenees themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; and (3) a reasonable expeetation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2142.

That any combination of Garvin with Rutter *et al.*, Ala-Kokko *et al.*, Maniatis *et al.*, Korfhage *et al.*, Lader, or Warrington *et al.*, as cited above, lacks a teaching or suggestion of the presently claimed invention is clear from the Graham analysis above.

Regarding motivation, the Supreme Court in KSR stated at Section C. p 15-16:

> "In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim."

Applicant submits that any combination of Garvin with Rutter *et al.*, Ala-Kokko *et al.*, Maniatis *et al.*, Korfhage *et al.*, Lader, or Warrington *et al.*, as cited above, does not render the subject matter set forth by the pending claims obvious, in part, because the combination of prior art references fails the "objective reach of the claims" test regarding "fractionating leukocytes from whole blood using a leukocyte depletion matrix; treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and (i) increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and (ii) reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition; and lysing the fractionated leukocytes to obtain a lysate comprising RNA and reduced gDNA contamination

compared to a lysate of fractionated leukoeytes that were not treated with the RNA preservation composition."

Regarding the expectation of success, it was not predictable that the results would show reduced genomic DNA (gDNA) contamination.

The Supreme Court in *KSR* stated at Section C. p17:

> "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning. ... Rigid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it."

Applicant notes that although there is a vast amount of knowledge about general relationships in the chemical and biochemical arts, chemistry and biochemistry are still largely empirical, and there is often great difficulty in predicting precisely how a given compound will behave. "Fractionating leukocytes from whole blood using a leukocyte depletion matrix; treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and (i) increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and (ii) reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition; and lysing the fractionated leukocytes to obtain a lysate comprising RNA and reduced gDNA contamination compared to a lysate of fractionated leukocytes that were not treated with the RNA preservation composition" is outside of the objective reach of any combination of art cited.

For the above cited reasons, Applicants submit that the invention as set forth by independent Claim 1 is patentable under U.S.C. §103 and respectfully requests that the rejection be withdrawn. An essential characteristic of a proper dependent claim is that it shall include every limitation of the claim from which it depends. Therefore, a dependent claim is allowable when the claim from which it depends is allowable. Claims 15, 23, and 24 have been cancelled. Claims 5, 6, 9, 12, 13, 16-22, 25, 27, 28, and 31-34 are dependent, either directly or indirectly on Claim 1. Therefore, Applicants submit that said claims are patentable also and respectfully request that the rejection under U.S.C. §103 be withdrawn.

Conclusion

Applicant believes that the application is in condition for allowance and respectfully requests the issuance of a Notice of Allowance. If the Examiner does not consider the application to bc in condition for allowance, Applicant requests the courtesy of a call to the undersigned at (512) 651-0595 to set up an interview.

PETITION FOR EXTENSION OF TIME AND FEE AUTHORIZATION

This document is a petition for a 3-month extension of time. The Commissioner is authorized to charge the fee for a 3-month extension of time for a small entity ($510.00) and any further fees due for the filing of the present document to Ambion Deposit Account No. 50-4140/6545 US. Any deficiency or overpayment should be charged or credited to this deposit account.

Respectfully submitted,

Date: June 26, 2007

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